

In the specification

Please insert the following paragraphs at page 16, line 5:

Depending upon the application, various types of sensors, for example, aptamers, antibodies/proteins, peptides, or high affinity ligands, can be linked to the uncapping/discharge mechanism of the nanocap-nanostructure-based assemblies of the invention. Thus, the uncapping mechanism can be linked to detection by the sensors on the nanocap-nanotube structure of surface markers on cells types (e.g., cancer cells), proteins in the blood (e.g., PSA for prostate cancer) or drugs in the body (e.g., illicit drugs or therapeutic drugs). These may or may not require the use of energy-bearing biomolecular motors such as, but not limited to, the actin-based system (Dickinson R. B. and Purich D. L., Biophys. J. 2002 82:605-617).

In another embodiment, the nanocap (or "end-cap") is attached by electrostatic attraction between the nanocap and the nanotube. The cap is released in response to a change in the ionic strength of the medium surrounding the nanotube. Alternatively, the cap can be held on by hydrogen bonding or by acid and/or basic sites on the nanocap/nanotube. The cap is released by a change in the pH or the surrounding medium. The cap may also be held on by covalent bonds that can be cleaved by a specific enzyme, for example, a hydrolase enzyme.

The sensors can be designed to initiate release of payload contents (such as a surrogate marker) upon detecting stimuli. Such stimuli can include physical stimuli, for example, the temperature, pressure, velocity or acceleration of the nanoparticle; biological stimuli, for example, the presence of normal or abnormal cell types, cellular surface antigens, proteins, oligonucleotides, or toxins; or chemical stimuli, for example, pH, ionic strength, hydration state, redox state, or the presence of therapeutic agents, or toxic drugs such as nerve agents.

For example, one can achieve safe and effective intracellular surrogate marker release by attaching the nanocap to the nanotube with covalent bonds (e.g., S--H bonds) that are broken when a specific chemical signal (e.g., high reducing atmosphere of the cytoplasmic environment of the interior of a mammalian cell) is encountered. The ability to incorporate different types of sensor mechanisms for removal of the cap is an extremely powerful approach to the delivery and

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release (or uptake) of payload contents in an event- and site-specific manner. Specifically, by linking the uncapping mechanism to various sensing modes, the nanotube based surrogate marker transport systems can be used to diagnose, treat, and monitor health status. For example, smart nanotubes can detect the appearance of cancer antigens on the walls of cancer cells, cause uncapping which in turn releases an indicator, which in turn makes the urine a distinct color or releases a nontoxic marker which can be readily detected in the breath, and thereby notifies the patient or his/her physician that a cancer cell(s) was encountered in his/her body.

Nanotube technology provides a method for delivering surrogate markers. In one embodiment, this is achieved using nanocaps that are firmly bound to the nanotube when the assembly is outside of the cell but are released, thus opening the nanotube and making the surrogate marker available, when the assembly is partitioned into the cell. For example, this can be accomplished using disulfide chemistry to couple the nanoparticle cap to the nanotube. The disulfide link between the nanotube and its nanocap is ideal because all living cells maintain a reducing environment within their cytoplasm. This contrasts with the oxidizing environment found outside the cell. The tripeptide glutathione (-glutamyl-cysteinyl-glycine) plays a key role in this process. In its reduced form, glutathione possesses a free sulfhydryl capable of reducing disulfide bonds, forming a disulfide-linked glutathione dimer in the process. This species, in turn, is reduced by nicotinamide-dependent enzymes.

Please insert the following paragraphs at page 18, line 26:

The end-cap (or "nanocap") can be used to impart several novel functions and degrees of intelligence to the nanotube-nanocap delivery system. These include the sealing of the payload contents (such as the surrogate marker) within the nanotube in a cost-effective manner.

The nanocap can also provide a mechanism whereby the nanotube payload contents can be selectively released. For example, when used for the in-vivo delivery of a surrogate marker, the nanotube can be designed to release its payload either at the surface of the target cell or within its cytoplasm. This may be achieved by sensing a chemical, physical or biological signal

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present in the local environment. Alternatively; a remote external energy source, such as ultrasonic irradiation, can be used to selectively release the payload from the nanotube. Time-controlled degradation of the biomaterials used to construct the nanotube and/or nanocaps can also provide a release mechanism.

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